

REMARKS

Reconsideration of the application is requested in view of the amendments to the claims and the remarks presented herein.

The claims in the application are claims 1 to 4, 7 to 21 and 34 to 42, all other claims being cancelled.

With respect to the withdrawn claims, it should be noted that claims 10 and 11 should be with the elected claims since they are dependent on claim 9 which is being examined with the elected claims. Therefore, they should be examined with the elected claims.

Claims 1 to 5, 7 to 9 and 34 to 42 were rejected under 35 USC 112, first paragraph as containing subject matter not described in the specification.

Applicants traverse this ground of rejection since claim 1 has been limited to the female steroids of former claim 6 which was subjected to this rejection.

Claims 1 to 9 and 12 to 14 were rejected under 35 USC 112, second paragraph since claims 12 and 13 referred to "the hormone" while claim 1 referred

to -- a compound-- and claim 14 lacked a period. Claims 1 to 9 were deemed unclear in “compounds capable of binding to hormone receptors”.

Applicants traverse these grounds of rejection since claims 12 and 13 now refer to a compound and claim 14 now has a period. Claim 1 has been amended to recite a Markhus group of specific compounds. Therefore, withdrawal of these rejections is requested.

Claims 34 and 35 are rejected under 35 USC 112, first paragraph as failing to comply with the enablement requirement as claims to prevention may be unbelievable absence very strong evidence since prevention is interpreted to mean that the disease/condition will entirely cease to manifest once the claimed compound/composition is administered. However, the Examiner believes there is no known method(s) for the determination of a person susceptible to said condition and, thus, in need of preventive treatment. Additionally, the Examiner states that the present specification lacks guidance and/or working examples of prevention of premature birth as recited by the claimed invention. Thus, in order to practice the claimed invention commensurate in scope with the instant claims, the skilled artisan according to the Examiner would have to search the prior art to find. If possible, a model for determining a person prone to having premature births and, thus, in need of preventive treatment.

Applicants traverse this ground of rejection since claim 1 has been limited in scope to a limited number of 3,5-dione compounds having a precise structure and common physical properties. The following experiments and facts supporting the evidence that several risk factors do influence the spontaneous preterm births observed. These clinical symptoms may be monitored and used to determine the women having a real risk of preterm birth. In these conditions, this treatment is not a preventive treatment, it is a treatment for women at risk.

Spontaneous preterm birth (PTB, delivery before 37 weeks gestation) is the result of either preterm labor with intact membranes or preterm premature rupture of the membranes. In 2002, 11.9% of U.S. births occurred before 37 weeks gestation. Epidemiologic studies have identified many demographic, behavioral, and medical characteristics associated with PTB risk. For instance, in the USA, risk factors for spontaneous preterm births include a previous preterm birth, black race, periodontal disease, low maternal body-mass index.

A critical review of potential risk factors has been published by Goffinet et al in 2005 (Goffinet F. Primary predictors of preterm labour. BJOG 2005; 112 (Suppl 1): 38-47). These risk factors are summarized in the following table:

<u>Risk Factors</u>	Association with spontaneous preterm birth
<u>Individual, socio-economic and behavioral</u>	
Domestic violence	++
Low social-economic status	++
Stress, depression, life events	++
Hard work	++
Gynaecological and obstetric history	
Preterm delivery or second trimester pregnancy loss	+++
Previous cone biopsy	+/-
Mullerian abnormalities	+
Family history (genetic factors)	+
Warning signs during prenatal surveillance	
IVF	+
Multiple pregnancy	+++
Placenta praevia	+++
Bleeding	++
Cervicovaginal infections	+
Uterine contractions	+
Cervical modifications	++

Recognized risk factors for preterm labor/preterm birth are also reported in a paper published in 2007 by NJ Reedy (Reedy NJ. Born too Soon: The Continuing

Challenge of Preterm Labor and Birth In the United States. *J Midwifery Womens Health* 2007; 52: 281-290). They are presented as follows:

Medical history:

History of birth \leq 37 completed gestational weeks

History of preterm premature rupture of membranes

History of threatened preterm labor

History of cervical surgery

Factors in present pregnancy:

Artificial reproductive technologies

Uterine anomaly

Short cervical length

Chronic urinary tract infection

Maternal socioeconomic stress

Smoking $>$ 1 pack of cigarettes per day

Substance abuse

Polyhydramnios

Multiple gestation

According to a more recent paper from Covarrubias in 2008 (Covarrubias LO, Aguirre GE, Chapuz JR, May AI, Velasquez JD, Eguiluz ME. Maternal factors associated to prematurity. *Ginecol Obstet Mex.* 2008; 76 (9): 526-36), premature

rupture of membranes and maternal morbidity during pregnancy are the most important risk factors of prematurity.

These authors have studied a cohort of live newborns in Mexico City since January 2000 to December 2004, with birth weight of 500g or higher. Prematurity prevalence was compared with and without risk factors. For each studied history it was calculated odds ratio (OR) with 95% confidence interval (95% CI).

Prematurity rate observed was 11.9%.

Most remarkable risk factors associated with prematurity are:

- illiterate mother (OR 1.54; 95% CI, 1.2-1.94),
- single mother,
- 36 years old or more (OR 1.81; 95% CI, 1.56-2.09),
- history of preterm delivery (OR 2.21; 95% CI, 1.54-3.16),
- multifetal pregnancy,
- obstetric morbidity (preeclampsia/eclampsia; OR 7.9; 95%CI, 6.6-9.4),
- gestational diabetes (OR 2.3; 95% CI, 1.75-2.92),
- urinary tract (OR 1.8; 95% CI, 1.56-1.96)
- vaginal infection, premature rupture of membranes, oligohydramnios,
- polyhydramnios (OR 4.48; 95% CI, 3.04-6.6),
- placenta previa, and
- abruption placentae (OR 9.96; 95% CI, 5.62-17.7).

In conclusion, it is crucial to carefully consider some medical conditions

associates to each individual pregnancy, such as

1) medical conditions

previous preterm delivery and previous premature rupture of membranes, multiple pregnancy, placenta praevia and abruptio placentae, uterine and cervical abnormalities, and infections.

2) socio-economical conditions

domestic violence, low social-economic status, stress depression, life events, hard work.

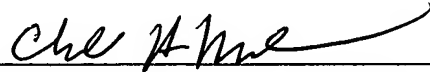
Therefore, it is deemed that claims 34 and 35 comply with 35 USC 112 and withdrawal of this rejection is requested.

Claims 1 to 5, 7 and 8 were rejected under USC 103 as being obvious over the Hodosan et al patent. The Examiner states that Hodosan et al teaches nitrate esters of steroid hormones including 3-ethoxyandrosta-3,5-dien-17 β -ol nitrate which is encompassed by the instant claims.

Applicants traverse this ground of rejection since Claim 1 has been limited to the compounds of former claim 6 as noted above and this claim was not rejected. Claims 9, 12 to 14 and 36 to 42 were not rejected on prior art and presumably these claims are drawn to allowable subject matter although the Examiner did not so state.

In view of the amendments to the claims and the above remarks, it is believed that the claims point out Applicants' patentable contribution. Therefore, favorable reconsideration of the application is requested.

Respectfully submitted,

A handwritten signature in cursive script, appearing to read "Charles A. Muserlian", written over a horizontal line.

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Enclosure